Laboratoire d'Optique et Biosciences
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Internship proposal:

Numerical simulations of coherent nonlinear microscopy in the cornea.

Nonlinear microscopy is an optical imaging method that relies on nonlinear optical contrasts. The most common nonlinear microscopy method is 2-photon excited fluorescence (2PEF) where 2 infrared photons are simultaneously absorbed by a fluorophore to emit a single visible photon. 2PEF is an incoherent process and therefore provides a simple image formation process where the signal detected in each voxel is proportional to the concentration of fluorophores in the corresponding focal volume. The situation is very different in the case of coherent nonlinear processes such as second harmonic generation (SHG) and Third Harmonic Generation (THG) where 2 (resp. 3) photons are simultaneously scattered by a molecule, to generate a single photon at twice (resp. three times) the frequency of the incoming laser photons. Since this scattering process is almost instantaneous, the phase information is maintained and therefore the signal detected per voxel is now a function of the number and strength of the harmonophores and of the phase relation between these emitters. This means that **the image formation process becomes highly non-trivial, especially when considering complex anisotropic materials and requires careful analysis.** In particular**, the human cornea** which is the front part of the eyeball and is very important for vision **consists in an array of collagen fibrils organized in a quasi-crystalline lattice**. The lab previously showed the potential of SHG and THG microscopy to study the micro organization of this structure in 3D [1,2] (Fig. 1).

This project aims at **modeling the SHG and THG response of the human cornea** and **use these numerical simulations to extract quantitative information from nonlinear images recorded recently by our group** (Fig. 1). Two approaches will be implemented, based on previous work at LOB [3]: (i) a semi-analytical approach based on Green's functions, which considers only nonlinear indices but with arbitrarily complex second and third-order tensors; (ii) a full numerical approach using Finite Difference Time-Domain (FDTD) to consider nanometer-scale heterogeneities in the refractive index that may affect the wave propagation.

The primary aim of this internship Iis to improve the existing Green's function code to develop more accurate models of the SHG response of the cornea, and to add third order tensors to this existing model to simulate the THG response. This project will take place in the "Advanced Microscopies" group at the Lab for Optics and Biosciences (LOB), located on the Polytechnique campus in Palaiseau. The LOB is an interdisciplinary lab with both physicists and biologists who develop together new approaches in optics, computational physics, image analysis, cell/developmental biology and biophysics to study biological systems.

This computational project is well suited for a Physics student with strong skills in Computational Physics and an interest in biology.

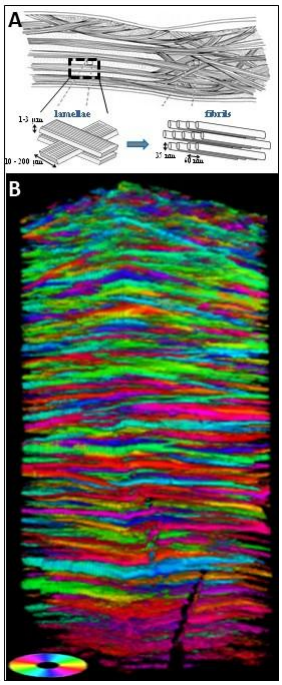


***Fig. 1** : A. multiscale structure of the Human cornea. B. pSHG mapping of the lamellar structure of the Human cornea (the color codes collagen orientation).*

Related recent publications (see also https://portail.polytechnique.fr/lob/):
[1] Aptel et al, IOVS. 51 (2010) - https://doi.org/10.1167/iovs.09-4586
[2] Raoux et al, Light Sci Appl 12 (2023) - 10.1038/s41377-023-01224-0
[3] Morizet et al, Optica 8 (2021) - 10.1364/OPTICA.421257

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See https://portail.polytechnique.fr/lob/recherche/advanced-microscopies-and-tissue-physiology